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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/830,451	07/31/2001	Louis Schofield	017227/0174	8055

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EXAMINER

DIBRINO, MARIANNE NMN

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 07/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/830,451

Applicant(s)

SCHOFIELD ET AL.

Examiner

DiBrino Marianne

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/17/01, 11/4/02 and 10/17/03.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-18 and 79-125 is/are pending in the application.
- 4a) Of the above claim(s) 4-8, 17, 79, 80, 89-99, 101, 107, 111-115 and 121-123 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9-16, 18, 81-88, 100, 102-106, 108-110, 116-120, 124 and 125 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendments filed 4/17/01 and 11/4/02 and Applicant's response filed 10/17/03 are acknowledged and have been entered.

Claims 1-18 and 79-137 are pending.

2. Applicant is reminded that claims 78-136 on pages 5-12 of the amendment filed 11/4/02 have been renumbered as claims 79-137 according to 37 CFR 1.126 because when claims are added, they must be numbered by the Applicant consecutively beginning with the number next following the highest numbered claim previously presented. It is requested that Applicant amend the dependent claims that recite a claim number to reflect the new numbering.

3. Applicant's election with traverse of Group I (claims 1-18 and 79-125), and species election of inducing an immune response, upregulation of the Th2 response, treatment or prophylaxis of the disease condition malaria using a GPI with the sequence EtN-P-[M α 2]M α 2M α 6M α 4G α 6Ino-Y in Applicant's response filed 10/17/03 is acknowledged.

The basis for Applicant's traversal is confined to the issue of upregulation of Th2 response alone. Applicant's position is that the present invention relates to an antibody response that involves both Th1 and Th2 responses, rather than a shift between the Th1 and Th2 responses.

It is the Examiner's position that the instant specification discloses activation of T helper cells wherein said activated T cells induce or otherwise upregulate a TH1-type response (page 8 at lines 26-31) OR wherein said activated T cells induce or otherwise upregulate a TH2-type response (page 9 at lines 1-7). In addition, the instant specification discloses that skewing towards induction of a Th2 response is desirable where a subject is suffering from cerebral malaria, for example (pages 35 and 36, paragraph spanning said pages), and that cerebral malaria is a Th1 driven pro-inflammatory disease (Example 21). It is the Examiner's position that the instant claims do not recite wherein the method of producing an antibody response that involves both Th1 and Th2 responses.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-3, 9-16, 18, 81-88, 100, 102-106, 108-110, 116-120, 124 and 125 read on the elected species.

Accordingly, claims 4-8, 17, 79, 80, 89-99, 101, 107, 111-115, 121-123 (non-elected species of Group I) and claims 78 and 126-137 (non-elected groups II and III) are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

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Claims 1-3, 9-16, 18, 81-88, 100, 102-106, 108-110, 116-120, 124 and 125 are currently being examined.

4. The disclosure is objected to because of the following informalities:

The use of the trademark Sepharose has been noted in this application, for instance on page 65 at line 7. It should be capitalized or accompanied by the TM or [®] symbol wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Each letter of the trademark must be capitalized. See MPEP 608.1(V) and Appendix 1.

Appropriate correction(s) is/are required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 9-16, 18, 81-88, 100, 102-106, 108-110, 116-120, 124 and 125 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the . . . claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed method of activating CD1-restricted Th (including CD1+ NK1.1+ T cells, Th2) cells comprising administration of a GPI derivative or equivalent thereof or complex thereof comprising or treatment or prophylaxis via administration of a GPI derivative or equivalent thereof or complex thereof

The instant claims encompass use of a derivative or equivalent of GPI to activate or induce Th cells in vitro or in vivo for treatment or for prophylaxis, including treatment or prophylaxis with GPI.

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The specification discloses that "derivatives" or "equivalents" should be understood to include reference to fragments, parts, portions, chemical equivalents, mutants, homologs and analogs, and further that equivalents may not necessarily be derived from GPI but may share certain conformational similarities, or alternatively, chemical equivalents may be specifically designed to mimic certain physiochemical properties of GPI and may also include synthetic carbohydrates and peptide mimetics (page 15 at lines 2-11).

The specification as filed does not provide written description support for derivative or equivalent; the skilled artisan cannot envision all the contemplated substances by the label "derivative" or "equivalents" and therefore conception cannot be not achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that it is part of the invention and along with a recitation of a function such as inducing Th cells. The derivative or equivalent itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

In addition, a definition by function does not suffice to define the genus because it is only an indication of what the property the peptide has, and if one extends the analysis in the instant case, what the peptide does (i.e., it induces a CD1-restricted Th cell response), rather than what it is. See Fiers, 984 F.2d at 1169-71, 25 USPQ2d at 1605-06. It is only a definition of a useful result rather than a definition of what achieves that result. Many such species may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin [e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One of ordinary skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

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7. Claims 1-3, 9-16, 18, 81-88, 100, 102-106, 108-110, 116-120, 124 and 125 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

The specification does not disclose how to practice the instant method comprising activating Th cells comprising administering a T cell activating amount of GPI or derivative or equivalent thereof or complex comprising any of these, nor how to practice the claimed method of inducing in a mammal an immune response directed to GPI, nor how to practice the claimed method of treatment and/or prophylaxis of a mammalian disease condition, including said condition characterized by microorganism infection such as those recited in the instant claims, including malaria. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass treatment and/or prophylaxis of any mammalian disease or condition with derivatives or equivalents of GPI that the specification does not disclose how to make and/or use, and/or treatment or prophylaxis of any mammalian disease condition, including those recited in the instant claims, with GPI, derivatives or equivalents.

The specification discloses that “derivatives” or “equivalents” should be understood to include reference to fragments, parts, portions, chemical equivalents, mutants, homologs and analogs, and further that equivalents may not necessarily be derived from GPI but may share certain conformational similarities, or alternatively, chemical equivalents may be specifically designed to mimic certain physiochemical properties of GPI and may also include synthetic carbohydrates and peptide mimetics (page 15 at lines 2-11).

The specification does not disclose any working examples of treatment or prophylaxis of any condition or disease in vivo, including in a mammal, comprising administration of GPI, derivatives or equivalents.

Evidentiary reference Schofield et al (Nature 2002, 418: 785-789) teaches that anti-GPI immunization prevents the development of pulmonary edema and acidosis as well as cerebral malaria in 75% of *P. Berghei* infection in mice, but vaccination did not prevent late-end stage infection characterized by overwhelming parasitemia associated with profound hemolytic anemia in mice and subsequent death (especially column one on page 788). Schofield et al further teach that the issue of whether GPI is a target of clinical immunity remains to be determined, that in contrast to acquired clinical immunity, anti-parasite immunity takes many more years to develop and is easily lost, reflecting the problems of antigenic diversity, antigenic variation, redundancy in invasion pathways, immune evasion strategies and genetic restriction in the immune response to parasite antigens (especially page 788 at column 2). Evidentiary reference Schofield et al teaches that although *P. berghei* is the best available model for certain aspects of lethal pathogenesis, it is not considered to model adequately these aspects of human malaria anemia, i.e., erythropoietic suppression (especially column 1 on page

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788).

Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 3 and 11-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 11 is indefinite in the recitation of "a-linkages" because it is not clear what is meant. It is suggested that Applicant amend said claims to recite " α -linkages" if that is what is meant.

b. Claim 3 is indefinite in the recitation of "wherein said CD4⁺ NK1.1⁺ T cell" because it is not clear what is meant. It is suggested that Applicant amend the said claim to recite "wherein said CD4⁺ T cell is a CD4⁺ NK1.1⁺ T cell".

10. For the purpose of prior art rejections, the filing date of the instant claims 11-13, 86-88, and 116-118 is deemed to be the filing date of the PCT application PCT/AU99/00929, i.e. 10/27/99, as the foreign priority application AU PP 6758 does not support the claimed limitations of the instant application. There is no disclosure of the chemical species recited in the said instant claims 11-13, 86-88 and 116-118 in the said foreign priority application.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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12. Claims 1-3, 9-18, 81-88, 100, 102-106, 108, 109, 116-120, 124 and 125 are rejected under 35 U.S.C. 102(b) as being anticipated by Schofield et al (J. Exp. Med. 1/93 177: 145-153) as evidenced by Nagata et al (Eur. J. Immunol. 1993 23: 1193-1196).

Schofield et al teach administration of *P. falciparum* GPI or analogues, including containing diacylglycerol, or from *T. brucei* (comprising phosphatidylcholine) in vivo for production of anti-GPI antibodies in the treatment of malaria (especially page 152, page 149, page 150). Schofield et al teach cerebral malaria is a type of malaria to be treated (especially page 152, column 2).

Evidentiary reference Nagata et al teaches that Th2 cells secrete IL-4, IL-5 and IL-6 and provide the major help for antibody production of T cells (especially first paragraph on page 1193).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. When a claim recites using an old composition or structure (e.g., GPI or analogues) and the use is directed to a result or property of that composition or structure (activating CD4⁺ NK1.1⁺ Th2 cells following administration for antibody production against GPI in treatment of malaria) then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. v. Milgram, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. v IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

13. Claims 11-13, 86-88 and 116-118 are rejected under 35 U.S.C. 102(a) as being anticipated by Schofield et al (Science 283: 225-229, 1/8/99) as evidenced by van Joost et al (J. Amer. Acad. Dermatol. 27: 922-8, 1992) and Paul (Fundamental Immunol. 2nd Ed., 1989, New York, Raven Press, page 405).

Schofield et al teach COOH-terminal GPIs from *P. falciparum* and *T. brucei* that have the same structure as the elected species, as well as GPIs from other sources such as parasitic protozoa (especially Figure 1 and page 228). Schofield et al further teach CD1-restricted recognition of GPI moieties, including those linked to diacylglycerol or alkylacylglycerol (especially paragraph 1, column 1 on page 227), by CD4⁺ NK1.1 Th cells, and production of high levels of IL-4 (involved in Th2 type responses). Schofield et al teach a method of activating or inducing T helper cells in vivo comprising administering GPI or a derivative or equivalent because Schofield et al teach administration of malaria to mice, and teach the use of GPI in vaccines to treat various pathogens such as malaria.

Evidentiary reference van Joost et al teaches that Th2 lymphocytes produce IL-4 (especially page 922), and evidentiary reference Paul teaches that Th2 cells produce IL-4 and that IL-4 induces IgG1 and IgE production from B cells.

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14. Claims 11, 13, 86, 88, 116 and 118 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 99/52547 (10/21/99).

WO 99/52547 teaches treatment of malaria or other parasitic infections comprising administering GPI to induce a CD4⁺ T cell response, including also inducing B cell activation through a T cell response, i.e., activation of CD4⁺ Th2 cells (especially page 3 at lines 9-21, pages 9-10, 12, 18, 19 and claims). WO 99/52547 teaches Plasmodium genus and species (especially pages 3, 10, 11 and 12 and claims). WO 99/52547 further teaches phospholipids such as phosphatidylinositol, phosphatidylethanolamine and phosphatidylglycerol (page 21). With regard to inclusion of claims 11, 86 and 116 in this rejection, claims 11, 86 and 116, recite "or derivatives or equivalents thereof".

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. When a claim recites using an old composition or structure (e.g., GPI) and the use is directed to a result or property of that composition or structure (activating CD4⁺ NK1.1⁺ Th cells following administration) then the claim is anticipated. See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. v. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. v. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

16. Claims 11-13, 86-88, 116-118 are rejected under 35 U.S.C. 103(a) as being obvious over WO 99/52547 (10/21/99) in view of Tachado et al (PNAS USA 94: 4022-4027, 4/97) and Joyce et al (Science 279: 3/6/98, pages 1541-1543).

WO 99/52547 teaches treatment of malaria or other parasitic infections comprising administering CD1-binding GPI to induce a CD4⁺ T cell response, including also inducing B cell activation through a T cell response, i.e., activation of CD4⁺ Th2 cells (especially page 3 at lines 9-21, pages 9-10, 12, 18, 19 and claims). WO 99/52547 teaches Plasmodium genus and species (especially pages 3, 10, 11 and 12 and claims). WO 99/52547 further teaches phospholipids such as phosphatidylinositol, phosphatidylethanolamine and phosphatidylglycerol (page 21). With inclusion of claims 11, 86 and 116 in this rejection, claims 11, 86 and 116, recite "or derivatives or equivalents thereof".

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WO 99/52547 does not teach the treatment of malaria or other parasitic infections comprising a GPI that comprises diacylglycerol.

Tachado et al teach GPI from *P. falciparum* malarial parasite that comprises diacylglycerol.

Joyce et al teach that GPI is a major natural ligand of CD1d1 that controls the function of NK1.1⁺ T cells.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the GPI taught by Tachado et al or by Joyce et al in place of the GPI taught by WO 99/52547 in the method taught by WO 99/52547.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to treat malaria.

17. No claim is allowed.

18. Applicant is requested to correct the spelling of "eaquivalent" and "wutg" in claim 1 at line 3 and the spelling of "Plasinodium" in claim 120 at line 2.

19. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Wednesday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Chan Y Christina, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Marianne DiBrino, Ph.D.

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